

## AMENDMENTS TO THE CLAIMS

1. **(Original)** An isolated, purified or recombinant complex comprising a POSH polypeptide and a POSH-associated protein (POSH-AP).
2. **(Original)** The complex of claim 1, wherein the POSH-AP is HERPUD1.
3. **(Original)** The complex of claim 2, wherein the HERPUD1 is ubiquitinated.
4. **(Original)** The complex of claim 2, wherein the HERPUD1 is monoubiquitinated.
- 5-15. **(Cancelled)**
16. **(Original)** A method of identifying an agent that inhibits a neurological disorder, comprising:
  - a) forming a mixture comprising a POSH polypeptide, a POSH-AP, ubiquitin and a test agent; and
  - b) detecting ubiquitination of the POSH-AP,wherein an agent that inhibits ubiquitination of the POSH-AP is an agent that inhibits a neurological disorder.
17. **(Original)** The method of claim 16, wherein the POSH-AP is HERPUD1.
18. **(Original)** The method of claim 16, further comprising testing the effect of the agent on POSH-mediated ubiquitination of a second substrate.
19. **(Original)** The method of claim 18, wherein the second substrate is POSH.
20. **(Cancelled)**

21. **(Currently Amended)** The method of claim 16[[20]], wherein the agent inhibits POSH-mediated ubiquitination of HERPUD1.
22. **(Original)** The method of claim 21, wherein the agent does not substantially inhibit POSH auto-ubiquitination.
- 23-25. **(Cancelled)**
26. **(Currently Amended)** The method of claim 16~~20 or claim 23~~, wherein the neurological disorder is selected from among: Alzheimer's disease, Parkinson's disease, Huntington's disease, Pick's disease, Niemann-Pick's disease, prion-associated diseases, depression, and schizophrenia.
27. **(Cancelled)**
28. **(Currently Amended)** The method of claim 16~~20 or claim 23~~, wherein said agent is selected from among: an siRNA construct, a small molecule, an antibody, and an antisense construct.
29. **(Cancelled)**
30. **(Currently Amended)** A method of identifying an agent to treat a neurological disorder, the method comprising identifying a test agent that disrupts a complex of claim 2~~any of claims 1-4~~.
31. **(Original)** The method of claim 30, wherein the neurological disorder is selected from among: Alzheimer's disease, Parkinson's disease, Huntington's disease, Pick's disease, Niemann-Pick's disease, prion-associated diseases, depression, and schizophrenia.
- 32-34. **(Cancelled)**
35. **(Original)** A method of testing an agent for use in treatment of a neurological disorder, comprising contacting cells that produce amyloid polypeptide with an agent that inhibits POSH activity and/or expression.

36. **(Original)** The method of claim 35, wherein the agent inhibits POSH ubiquitin ligase activity.
37. **(Original)** The method of claim 36, wherein the agent inhibits the ubiquitination of HERPUD1.
38. **(Original)** The method of claim 35, wherein the agent inhibits the expression of POSH.
39. **(Original)** The method of claim 35, wherein the agent is selected from among: an siRNA construct, a small molecule, an antibody, and an antisense construct.
40. **(Original)** The method of claim 35, further comprising evaluating the effect of the agent on apoptosis in the cell.